

REMARKS

In item 1, page 2 of the Office Action, the Office acknowledges that claims 67-115 were being examined and subject to restriction. Claims 81-85 and 87-93 are directed to a separate non-elected invention. Claims 94, 97-103, 110-112, and 115 have been cancelled. Accordingly, only claims 67-80, 86 and 95-96, 104-109, and 113-114, are being examined.

Applicants have amended claims 67-80, 86, 95-96, 104-108, and 113-114, herein. The changes in claims 67-80, 86, 95-96, 104-108, and 113-114, do not involve new matter, and are supported by the specification as originally filed. Entry of these amendments is respectfully requested.

RESTRICTION REQUIREMENT

In item 2, page 2 of the Office Action, the Office made final the restriction requirement and Applicants' election of Group I. Applicants are pleased that the Office will include claim 86 in elected Group I, since claim 86 recites a CTLA4 mutant molecule. The Office further takes the position that claims 81-85 and 87-93 are directed to a non-elected invention and are deemed withdrawn.

INFORMATION DISCLOSURE STATEMENT (IDS)

In item 3, page 2 of the Office Action, Applicants' IDS's are acknowledged. Applicants thank the Office for placing a line through duplicate citations in previously filed IDS's.

Applicants also understand the Office has placed a line through some citations listed in an IDS filed November 13, 2002, because the Office deemed them to be inappropriate for listing on the face of a patent. Applicants thank the Office for suggesting Applicants use

the procedures set forth in MPEP §724.02 for filing future proprietary information relevant to examination of the present application.

The Office has requested Applicants provide pertinent information regarding Exhibit 57 (slides 1-20) of Applicants' IDS submitted June 19, 2001. For the Office's convenience, Applicants attached a copy of Exhibit 57 as originally filed in the IDS dated November 13, 2001, which is annotated to indicate the slide numbers (annexed herewith as Exhibit B).

In response to the Office's request, Applicants note that slides 1, 3-11, and 13-20 of Exhibit 57 were presented at the Canadian Society of Transplantation Annual Scientific Meeting in Mont Tremblant, Quebec, Canada, on March 3-4, 2000. Slides 2 and 12 were presented at the American Society of Transplantation Meeting in Las Croabas, Puerto Rico on January 13-17, 2000.

PRIORITY

In item 4, page 3 of the Office Action, Applicants are pleased that the Office considers the provisional applications U.S. Serial No. 60/287,576 and U.S. Serial No. 60/214,065, provide adequate written support for the instant claims.

SPECIFICATION

In item 5, page 3 of the Office Action, the Office is requesting the Applicants review the specification for typographical errors and omissions, such as Sequence Identifier numbers. Applicants have complied.

CLAIM OBJECTIONS

In item 6, page 3 of the Office Action, the Office is requesting correction of claim 67, i.e., insert a colon after 'SEQ ID NO'. Applicants have complied.

In item 7, page 3 of the Office Action, the Office is requesting correction of claim 71, i.e., delete the duplicate 'amino acid'. Applicants have complied.

In item 8, page 3 of the Office Action, the Office is requesting correction of claims 97-115, i.e., recite 'SEQ ID NO' in the claims. Applicants have complied where appropriate. Claims 97-103, 110-112, and 115 have been cancelled and claims 104-109 and 113-114 now depend on claim 71.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

In items 9 and 10, at page 3 of the Office Action, the Office rejects claims 86, 94-96 and 115, under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to use the invention. In particular, the Office contends that the DNA composition of the present invention is a required element to practice the invention. Accordingly, the Office is requiring Applicants to provide assurance that the ATCC deposit of the DNA composition be made readily obtainable to the public. The Office states that Applicants can obviate this rejection by providing assurance of the availability of the deposit and a showing that the deposit was made under the terms of the Budapest Treaty.

In response, Applicants provide the following statement of assurance.

Statement of ATCC Deposit:

Applicants' patent representative maintains that the plasmid DNA disclosed in the present application is the same as that designated ATCC Accession No. PTA-2104 which has been deposited pursuant to the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure with the Patent Culture Depository of the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, Virginia 20110-2209 U.S.A. on June 19, 2000. Applicants provide a copy of a Receipt Form issued by the American Type Culture Collection, confirming deposit of the above-mentioned plasmid DNA (Exhibit A).

Accordingly, Applicants maintain that during the pendency of the present application, access to the ATCC deposit will be afforded to one determined by the Commissioner to be entitled thereto under 35 U.S.C. §1.14 and §122, and all restrictions on the availability to the public of the material deposited under ATCC Accession No. PTA-2104 will be irrevocably removed upon the issuance of a patent from the present application. Furthermore, the above deposits will be maintained by the ATCC for a period of 30 years from the date of deposit or at least 5 years after the last request for a sample of the deposited material, whichever is longer. Where the ATCC cannot furnish samples of the above deposits for any reason, Applicants shall make a replacement deposit, of the material which was originally deposited, within three months of receiving notification that the ATCC cannot furnish samples.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §102(b)

In items 11 and 12, at page 4 of the Office Action, the Office rejects claims 67-80, 86 and 94-115, under 35 U.S.C. §102(b), as allegedly anticipated by WO 98/33513 (Peach, et al.), as evidenced by US 2003/0083246 A1 (Cohen, et al.).

Applicants respectfully disagree with the rejection. In rejecting the claims, the Patent Office acted contrary to the guidance provided by the Federal Circuit, as to how to evaluate novelty with respect to the prior art.

The Legal Standard for Novelty:

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). Each and every element of the claimed invention must be disclosed in a single prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the invention in possession of the public. *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied* 469 U.S. 851, 105 S. Ct. 172 (1984); *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576-7 (Fed. Cir. 1991), *clarified, on recons.*, 1991 U.S.App. LEXIS 33,486 (Fed. Cir. 1991). The absence of even a single element from a prior art reference negates anticipation. *Atlas Powder Co. v. E. I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1574 (Fed. Cir. 1984).

It is sometimes permissible to use additional references to show evidence of inherent anticipation (MPEP 2131.01). However, “while it is sometimes appropriate to consider extrinsic evidence to explain disclosure of reference, such factual elaboration is necessarily of limited scope and probative value, for finding of anticipation requires that all aspects of claimed invention were already described in single reference, a finding that is not supportable if it is necessary to prove facts beyond those disclosed in reference in order to meet claim limitations” (*Scripps Clinic & Research Found. V. Genentech, Inc.*, 927 F.2d 1565, 176 (Fed. Cir. 1991)).

According to MPEP §2131.01, the reliance on an extra reference is proper only if cited to:

- (A) Prove the primary reference contains an "enabled disclosure;"
- (B) Explain the meaning of a term used in the primary reference; or
- (C) Show that a characteristic not disclosed in the reference is inherent.

Applicants Have Met the Legal Standard for Novelty:

Peach et al. (WO 98/33513) does not expressly or inherently anticipate the presently claimed mutant CTLA4 molecule:

- a. The amino acid and nucleic acid sequences of the mutant CTLA4 molecules of Peach et al. (WO 98/33513) are different from what is claimed*

As the Office correctly states, Peach et al. (WO 98/33513) disclose mutant CTLA4 molecules having amino acid sequences which **differ** from that of the presently claimed mutant CTLA4 molecule.

Peach et al. (WO 98/33513) teach mutant CTLA4 molecules having mutations at positions 29 and 106, as shown in Figure 7 of Peach et al. (WO 98/33513). Using a single-letter, amino acid code based on the numbering system of Figure 7 of the present application, the prior art molecule of Peach et al. (WO 98/33513) is designated, e.g., as G105EK28YIg.

In contrast, the presently claimed CTLA4 mutant molecule has mutations at:

- (1) position 29, as shown in Figure 7 of the present application, (position 55 of SEQ ID NO:4) which corresponds to position 30 of Figure 7 of Peach et al. (WO 98/33513), and
- (2) position 104, as shown in Figure 7 of the present application, (position 130 of SEQ ID NO:4) which corresponds to position 105 of Peach et al. (WO 98/33513).

Using the same single-letter, amino acid code based on the numbering system of the present application, the presently claimed CTLA4 mutant molecule is designated L104EA29YIg. As the Office concedes, one skilled in the art will recognize that the sequence of the Peach et al. (WO 98/33513) mutant molecule (e.g., G105EK28YIg) differs from that of Applicants' presently claimed molecule (e.g., L104EA29YIg).

Applicants have met the legal standard for novelty, because the single reference of Peach et al. (WO 98/33513), does not *identically* disclose a claimed soluble CTLA4 mutant molecule comprising an extracellular domain of CTLA4 as shown in SEQ ID NO:8 beginning with alanine at position 26 or methionine at position 27 and ending with aspartic acid at position 150, or a portion thereof, wherein in the extracellular domain or portion thereof an alanine at position 55 is substituted with a tyrosine, and a leucine at position 130 is substituted with a glutamic acid. Accordingly, Peach et al. (WO 98/33513) does not expressly anticipate the presently claimed invention.

b. Peach et al. (WO 98/33513) does not enable the presently claimed invention

Peach et al. (WO 98/33513) cannot be enabling for the claimed invention, since it is uncontroverted that Peach et al. (WO 98/33513) does not disclose the presently claimed CTLA4 mutant molecule.

To be enabling under Section 112, a patent must contain a **description** that enables one skilled in the art to make and use the claimed invention (*Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984)). One cannot enable what one cannot adequately describe. To adequately describe the presently claimed mutant CTLA4 molecule, one must disclose the exact sequence (An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; *what is required is a description of the DNA itself* (*Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993))).

c. Cohen does not support that the teachings of Peach et al. (WO 98/33513) inherently disclose the claimed invention

Cohen is an improperly cited additional reference under 35 U.S.C. §102(b), as set forth in MPEP §2131.01, because Cohen does not,

- 1) prove that Peach (WO 98/33513) contains an "enabled disclosure," with respect to the presently claimed mutant compounds;
- 2) explain the meaning of a term used in Peach (WO 98/33513) relevant to anticipation by Peach (WO 98/33513) of the claimed mutant compounds, or
- 3) show that a characteristic, relevant to the claimed invention, not disclosed in Peach (WO 98/33513), is inherent.

First, Cohen does not prove that Peach (WO 98/33513) contains an enabling disclosure because, although Cohen, like Peach (WO 98/33513), refers to its sequence as LEA29Y, the sequences in Cohen and Peach (WO 98/33513) are different. In actuality, Cohen et al. disclose that their claimed methods include the use of e.g., L104EA29YIg, which in Example 3 of the Cohen reference is also referred to as LEA29Y (Cohen at page 19, paragraph 237). Regardless of the designation of the different sequences as LEA29Y, the actual DNA and amino acid sequences disclosed in either reference enables only that exact sequence. In order to anticipate the presently claimed mutant molecule, Peach (WO 98/33513) must disclose the exact sequence of the molecule. The fact that a later filed reference, i.e., the Cohen reference, discloses the same sequence as the presently claimed molecule, cannot be used to substitute for the **different** molecule disclosed in Peach et al. (WO 98/33513) notwithstanding the fact that both Peach et al. (WO 98/33513) and Cohen designate the two different sequences as "LEA29Y."

Second, Cohen does not explain the meaning of the term "LEA29Y" used in Peach (WO 98/33513). "LEA29Y" having the sequence shown in Figure 7 of the Peach reference (WO 98/33513), is different than the L104EA29YIg, also referred to as "LEA29Y,"

having the sequence shown in Figure 7, of the Cohen reference. The name given a molecule or compound is not its definition or description. What is required, in the case of DNA is the sequence or structure of the moiety. (*Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993)). A cDNA is not defined or described by the mere name "cDNA" even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA (*The Regents of the University of California v. Eli Lilly and Company*, 119 F.3d 1559, 1568-1569 (Fed. Cir. 1997)).

Third, Cohen does not show that a characteristic, namely, the differences in the sequences, not disclosed in Peach (WO 98/33513), is inherent. Respectfully, Applicants contend the fact that the Cohen reference, which is **not** prior art, discloses the same sequence as the presently claimed molecule, cannot be used to substitute for a **different** molecule disclosed in the cited Peach et al. (WO 98/33513) reference notwithstanding the fact that both Peach et al. (WO 98/33513) and Cohen designate the two different sequences as "LEA29Y." The actual sequence defines the molecule of Peach (WO 98/33513), not its name.

Further, unlike the molecule of Peach et al. (WO 98/33513), in the present application, a nucleic acid molecule that encodes a claimed mutant CTLA4 molecule, L104EA29YIg, was deposited on June 19, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 (designated ATCC No. PTA-2104).

For these reasons, Applicants request the Office withdraw the art rejections under 35 U.S.C. §102(b).

DOUBLE PATENTING

In items 13 and 14, at page 5 of the Office Action, the Office provisionally rejects claims 67-80, 86 and 94-115 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 26-31 and 34-39 of copending application U.S. Serial No. 09/898,195.

This rejection is presently untimely. Applicants will gladly revisit this issue upon allowance of subject matter in the present case.

OWNERSHIP OF THE INVENTIONS

In item 15, at page 5 of the Office Action, the Office states that the question of common ownership of the present application and U.S. Serial No. 09/898,195 (e.g., '195 application) must be resolved in order to determine if a rejection under 35 U.S.C. §103(a) or §102(f) or (g) should be issued.

The Office requires Applicants to show the inventions of the present application and '195 application were commonly owned at the time the subject invention was made.

In response, Applicants respectfully contend that this rejection is inappropriate in this case because the present application is earlier filed than U.S. Serial No. 09/898,195. The '195 application is not prior art to the present application and thus cannot be the basis for a 102 or 103 rejection. Applicants will gladly comply with this requirement in an appropriate application.

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
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CONCLUSION

If a telephone interview would be of assistance in advancing prosecution of the present application, Applicants' undersigned attorney invites the Examiner to telephone her at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. If any fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Respectfully submitted,



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